Application No.: 10/576,496

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the

application:

LISTING OF CLAIMS:

1. (withdrawn): A method for obtaining a disease-associated gene, wherein a

disease-associated transcription factor is expressed in a cell line that is deficient in said

transcription factor or in a primary cultured cell, and the gene the expression of which is thereby

induced or inhibited is screened.

2. (withdrawn): The method according to claim 1, wherein the disease-associated

gene is a Runx2/Cbfa1-related disease-associated gene, and wherein Runx2/Cbfa1 is expressed

in a Runxs/Cbfa1-deficient chondrocyte cell line or in a Runx2/Cbfa1-deficient primary cultured

cell, and the gene the expression of which is thereby induced or inhibited is screened.

(withdrawn): The method according to claim 2, wherein the Runx2/Cbfa1-

related disease-associated gene is a gene associated with regulation of cartilage differentiation,

and wherein Runx2/Cbfa1 is expressed in a Runx2/Cbfa1-deficient chondrocyte cell line or in a

Runx2/Cbfa1-deficient primary cultured cell, and the gene the expression of which is thereby

induced or inhibited is screened.

4. (withdrawn): The method according to any one of claims 1 to 3, wherein said

screening is carried out via subtraction or DNA chip analysis.

Application No.: 10/576,496

5. (currently amended): A primary chondrocyte or cultured chondrocyte cell line

derived from a Runx2/Cbfa1-deficient mouse.

6. (currently amended): A chondrocyte <u>cell line</u> derived from a Runx2/Cbfa1- and

p53-deficient mouse.

7. (original): The chondrocyte cell line derived from the Runx2/Cbfa1- and

p53-deficient mouse according to claim 6, which is the RU-1 cell line or the RU-22 cell line

deposited under the accession number FERM BP-10137 or FERM BP-10138 at the International

Patent Organism Depositary of the National Institute of Advanced Industrial Science and

Technology.

8. (canceled).

9. (withdrawn): A polynucleotide having the nucleotide sequence shown in SEQ

ID NO: 9.

10-14. (canceled).

15. (withdrawn): A human homolog polynucleotide of the polynucleotide according

to claim 9, which has the nucleotide sequence shown in SEQ ID NO: 35.

Application No.: 10/576,496

16. (withdrawn): A polynucleotide having 65% or more homology to the

polypeptide encoded by the polynucleotide having the nucleotide sequence shown in SEQ ID

NO: 9 or 35, and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

17. (withdrawn): A polynucleotide being capable of hybridizing under stringent

conditions to the polynucleotide having the nucleotide sequence shown in SEQ ID NO: 9 or 35

or a complementary strand thereof, and encoding a protein capable of stimulating or inhibiting

cartilage differentiation.

18. (withdrawn): A recombinant DNA vector comprising the polynucleotide

according to any one of claims 9, 15, 16, and 17 or a complementary strand thereof.

19. (withdrawn): A transformant transformed with the recombinant DNA vector

according to claim 18.

20. (withdrawn): A polypeptide comprising the amino acid sequence shown in SEQ

ID NO: 10.

21. (withdrawn): A polypeptide comprising an amino acid sequence derived from

the amino acid sequence shown in SEO ID NO: 10 by deletion, substitution, or addition of one or

several amino acid residues, and capable of stimulating or inhibiting cartilage differentiation.

Application No.: 10/576,496

22. (withdrawn): A polypeptide comprising an amino acid sequence having at least 65% homology to the amino acid sequence shown in SEO ID NO: 10, and capable of stimulating

or inhibiting cartilage differentiation.

23-30. (canceled).

31. (withdrawn): A pharmaceutical composition comprising the polynucleotide

having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51,

a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide

sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a

protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being

capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID $\,$

NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or

inhibiting cartilage differentiation, and a pharmaceutically acceptable carrier.

32. (withdrawn): A method for preventing and/or treating a bone and/or joint

disease comprising administering to a subject the polynucleotide having the nucleotide sequence

shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65%

or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO:

1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or

inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under

stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29,

Application No.: 10/576,496

31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

- (withdrawn): The method according to claim 32, wherein the bone and/or joint disease is osteoarthritis.
- 34. (withdrawn): A method for diagnosing a disease comprising contacting a sample with the polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation.
- 35. (withdrawn): A method for diagnosing a bone and/or joint disease comprising contacting a sample with the polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation.

Application No.: 10/576,496

36. (withdrawn): The method according to claim 35, wherein the bone and/or joint disease is osteoarthritis.

- 37. (withdrawn): A transgenic animal model of a bone and/or joint disease, in which an expression level of the gene encoded by the polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation is enhanced or lowered.
- 38. (withdrawn): A transgenic mouse model of a bone and/or joint disease, in which the gene encoded by the polynucleotide having the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51, a polynucleotide having 65% or more homology to the polypeptide encoded by the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation, or a polynucleotide being capable of hybridizing under stringent conditions to the nucleotide sequence shown in SEQ ID NO: 1, 3, 5, 9, 15, 25, 27, 29, 31, 35, 41, or 51 and encoding a protein capable of stimulating or inhibiting cartilage differentiation is expressed with the use of a type II collagen promoter.

Application No.: 10/576,496

39-94. (canceled).